REMARKS

The non-elected claims are cancelled without prejudice and claims 24-27, 37, 38 and 45 dependent on non-elected claims are cancelled without prejudice. Claim 49 is amended to more clearly define the invention. Support for the amendment is found in the originally filed claims. No new matter has been introduced. Entry of the amended claims is requested.

RESPONSE

The claims now pending are 1, 4-7, 10-14, 21, 32, 35-36, 43-44 and 46-49.

The Examiner has rejected all of the elected claims 1, 4-7, 10-14, 21, 24-27, 32, 35-38, 43-49 as being unpatentable on several grounds. Reconsideration of the rejection is requested in view of the amended claims and the reasons stated for each of the grounds as follows.

Rejection under 35 U.S.C. §101

All of the pending claims were rejected for lacking in utility. It is the Examiner's contention that the specification for failure to provide sufficient description to support a credible utility.

The rejection is traversed. The pending claims 1, 4-7, 10-14, 21, 32, 35-36, 43-44 and 46-49 are directed to isolated nucleic acids encoding *elk*1, *elk*2 and *eag*2, each of which is an alpha subunit of a eag-like potassium channel, a method of isolating said nucleic acids, expression vectors comprising said nucleic acids and host cells comprising the expression vectors.

The utility of the claimed nucleic acids is for the expression of the potassium channel alpha subunits: *elk*1, *elk*2 and *eag*2.

There is a substantial body of literature on potassium channels and their functions in cardio vascular health. Applicants provided an extensive list of references that relates to potassium channels. In particular, it is known that there are three main classes of potassium channels: six-transmembrane (6TM), four-tansmembrane (4TM) and two transmembrane (2TM) subunits. The alpha subunits, *elk*1, *elk*2 and *eag*2, of the present invention belongs to a family referred to as the

ether-a-go-go (EAG) family under the 6TM superfamily. They are voltage sensitive K channels that attenuates the efflux of potassium ions during depolarization. Because they are slowly activated outward rectifying, they are significant in maintaining the resting potential of a cell.

It is known that the EAG-like proteins under the 6TM superfamily regulate the transport of potassium ions across cell membranes. It is also known that the 'channels' must operate properly to maintain health. *erg*1 is known and its function in connection with regulating of potassium ion concentration have been determined. It is also known that mutations therein leads to a disease known as Long QT syndrome, giving rise to cardiac arrhythmia and may even lead to sudden death. In the present application, it is shown that the proteins *elk*1, *elk*2 and *eag*2 encoded by the claimed polynucleotides belong to the subfamily of 6TM potassium channels that includes *erg*1, *elk*1, *elk*2 and *eag*2 and is expected to function like *erg*1.

The availability of the claimed polynucleotides encoding *elk*1, *elk*2 and *eag*2, enables expression of these polypeptides. The polypeptides are useful for screening for modulators, activators and inhibitors of inward rectifying potassium channels. The modulation of the channels is useful for the treatment of a variety of disease states associated with abnormal potassium channel activities, which lead to hypertension, acute and chronic renal failure, diabetes, abnormal thyroid activity, cystic fibrosis, etc. See page 16, line 29 – page 17 line 16.

In addition to sharing the characteristics of the EAG subfamily of potassium channels, there is specific, substantial utility of *elk*1, *elk*2 and *eag*2 because they can be used as reporter molecules for measuring potassium concentration, a strong indicator of hypertension and/or renal failure. See page 17, line 17 – page 18, lie 11.

The diagnosis of a disease condition itself is a substantial utility. This utility is credible to those of skill in the art. Attached hereto is a Declaration by Dr. Douglas Krafte, who is skilled as molecular neurobiology with substantial experience in this field. He has read the present specification, including the data presented in the drawings Figures 4A – 4H. In his opinion, the detailed description of the specification of this application provides information that supports the utility of the claimed invention. Specifically, he points to Figures 4G and 4H as evidence that the

elk and eag channels are useful in for identifying drugs that selectively interact with the different ion channels. See paragraphs 6 and 7. Dr. Krafte pointed out that the availability of single subunits are useful to identify agents, which are active on native channels.

The issue is whether the disclosed and claimed polynucleotides are useful to express proteins that are useful. Based on the data that shows that the *elk*1, *elk*2 and *eag*2 have properties that shows that they belong to the class of proteins in a subfamily under the superfamily 6TM. This class of proteins have known functions. To one of skill in the art, this is sufficient to show that these proteins have substantial, and specific uses. The uses are credible. This is enough.

The Examiner has regarded the use of the claimed *elk*1, *elk*2 and *eag*2 channels for the screening of drugs as being not real, insubstantial and not credible, and does not support the utility requirement under §101. Whether the data provided meets with the utility requirements under §101 is determine from the point of view of a person of skill in the relevant art. According to Dr. Krafte, who is a person of skill in the neurobiological art, the information presented in the whole specification supports the claims of the present invention.

In addition to the use of the claimed invention in screening drugs for modulating potassium channel activity, the assertion of the claimed invention for the expression of *elk*1, *elk*2 and *eag*2 for use as reporter molecules for measuring potassium efflux. Irregularity of potassium efflux has been associated with hypertension, renal failure, diabetic nephropathy, hypo or hyperthyroidism, goiter, etc. This information shows a real world specific, substantial and credible utility. See Page 17, line 16 et seq. This does not appear to have been considered by the Examiner. Based on the statements of Dr. Krafte and the specific, credible and substantial utility of the claimed invention for use in assaying potassium concentration in body fluids for the diagnosis of hypertension, renal failure and/or diabetes, reconsideration of the rejection on this ground is requested.

Furthermore, the Examiner cited Curtis US 6,518,398 as a reference. A review of the specification found similar description of the utility of erg-LP nucleic acid molecules and the expression thereof. The utility described included, use of the

expression product in screening for modulators, in detection assays, tissue typing, etc. There is no showing demonstrating the alleged use of the expressed proteins. In fact, the Curtis specification did not even provide any data on the electrophysiological characteristics as presented in Figures 4A – 4H. It would appear that the standard for determining specific, credible well established utility had not been applied in the same manner. For this reason, the rejection on this basis should be reconsidered.

Rejection under 35 U.S.C. §112. first paragraph

The pending claims were also rejected as being not supported by the specification for the same reasons stated for the rejection under 35 U.S.C. §101.

Reconsideration of the rejection is requested also for the same reasons stated above.

Rejection under 35 U.S.C. §112. second paragraph

Claims 12-14 were rejected for being indefinite in not providing the metes and bounds for the terms "stringent hybridization", "specifically hybridizes" and "moderately stringent hybridization."

A review of claim 12-14 show that claims 12 and 13 do not refer to hybridization. Whereas, the term "stringent hybridization" is recited in claims 14 and 21. It is assumed that the rejection is applicable to claims 14 and 21 and not 12 or 13.

The term is specifically defined in the specification at page 36. "specifically hybridize" means hybridization under stringent hybridizing conditions, which is in turn defined at page 36, line 12-page 37, line 11. These definitions are well known to those of skill in the art. See Techniques in Biochemistry and Molecular Biology (1993). The specification clearly provides the conditions for stringent hybridization: a temperature of 5-10°C lower than the thermal melting point for the nucleic acid. The temperature is at which 50% of the probes bind to the target at equilibrium. The salt concentration is less than 1.0 M Na ion concentration at pH of 7 to 8.3. Specific stringent conditions are also provided listing the following 50% formamide,, 5X SSC, 1% SDS with incubation at 42°C; or 5X SSC, 1% SDS, incubating at 65°C with a wash in 0.2X SSC and).1% SDS at 65°C. The definition of stringent hybridization

condition and specific hybrization and the detailed description of hybridization conditions in Examples on page 49, claims 14 and 21 are clear and distinctive. The objection to claims 14 and 21 on this basis should be reconsidered and withdrawn.

Priority

The Examiner appear to have denied the claim to priority to the filing date of the provisional application on the ground that the provisional application fails to provide adequate support for the pending claims. The Examiner relied on the reasons stated for rejecting the pending claims for lack of support under 35 U.S.C. §112.

Applicants request reconsideration for the same reasons stated above and points out that the description in the specification amply supports the claimed polynucleotides and the different types of utility asserted is enabling to those of skill in the art.

Rejection under 35 U.S.C. §102(e)

All of the pending claims are rejected as being anticipated by Curtis.

A review of Curtis shows that it is a continuation-in-part application of an earlier application filed July 21, 1998. Without reviewing the earlier filed application to determine the effective date of Curtis, Applicants is assuming without prejudice that Curtis is entitled to claim priority to July 21, 1998. The present application was filed as a provisional application on August 31, 1998.

The undersigned has reviewed the application. The data obtained and presented in the provisional application clearly indicates that the work on the claimed invention began prior to July 21, 1998. This was also discussed with one of the co-inventors, Dr. David McKinnon. He has stated that the work on the invention began prior to July 21, 1998 and was diligently reduced to practice. The invention was disclosed to the Applicants' attorney on August 20, 1998 and the prior application was filed on August 31, 1998. A declaration has been provided to Dr. McKinnon for his review and signature. Unfortunately, Dr. McKinnon is not well and has not been able to locate the notebook recording the work done. As soon as the record is located, a signed declaration will be submitted to supplement this response. Based on these facts, Curtis is not an effective reference.

CONCLUSION

No other issues were raised. It is believed that the claims as amended are allowable and an early allowance is requested.

Respectfully submitted,

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